

TECH CENTER 1600/2900

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 Xu, Xiang
 Huang, Betty

<120> Tankyrase H, Compositions Involved in the Cell Cycle and Methods of Use

<130> A-68292-2/RMS/DHR

<140> US 09/843,159

<141> 2001-04-25

<150> US 09/696,668

<151> 2000-10-25

<150> US 09/427,154

<151> 1999-10-25

<160> (17)

<170> PatentIn version 3.1

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245

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Lys Glu Arg Leu Ala Tyr Glu Phe Lys Gly His Ser Leu Leu Gln Ala 265 Ala Arq Glu Ala Asp Val Thr Arg Ile Lys Lys His Leu Ser Leu Glu 280 Met Val Asn Phe Lys His Pro Gln Thr His Glu Thr Ala Leu His Cys 295 Ala Ala Ser Pro Tyr Pro Lys Arg Lys Gln Ile Cys Glu Leu Leu 310 315 Leu Arg Lys Gly Ala Asn Ile Asn Glu Lys Thr Lys Glu Phe Leu Thr 330 325 Pro Leu His Val Ala Ser Glu Lys Ala His Asn Asp Val Val Glu Val 340 345 Val Val Lys His Glu Ala Lys Val Asn Ala Leu Asp Asn Leu Gly Gln 355 360 Thr Ser Leu His Arg Ala Ala Tyr Cys Gly His Leu Gln Thr Cys Arg 370 Leu Leu Ser Tyr Gly Cys Asp Pro Asn Ile Ile Ser Leu Gln Gly 390 395 Phe Thr Ala Leu Gln Met Gly Asn Glu Asn Val Gln Gln Leu Leu Gln Glu Gly Ile Ser Leu Gly Asn Ser Glu Ala Asp Arg Gln Leu Leu Glu Ala Ala Lys Ala Gly Asp Val Glu Thr Val Lys Lys Leu Cys Thr Val 435 Gln Ser Val Asn Cys Arg Asp Ile Glu Gly Arg Gln Ser Thr Pro Leu 450 His Phe Ala Ala Gly Tyr Asn Arg Val Ser Val Val Glu Tyr Leu Leu 465

Gln His Gly Ala Asp Val His Ala Lys Asp Lys Gly Gly Leu Val Pro

Leu His Asn Ala Cys Ser Tyr Gly His Tyr Glu Val Ala Glu Leu Leu

Boot.

500 505 510

Val Lys His Gly Ala Val Val Asn Val Ala Asp Leu Trp Lys Phe Thr 515 520 525

Pro Leu His Glu Ala Ala Ala Lys Gly Lys Tyr Glu Ile Cys Lys Leu 530 535 540

Leu Leu Gln His Gly Ala Asp Pro Thr Lys Lys Asn Arg Asp Gly Asn 545 550 555 560

Thr Pro Leu Asp Leu Val Lys Asp Gly Asp Thr Asp Ile Gln Asp Leu 565 570 575

Leu Arg Gly Asp Ala Ala Leu Leu Asp Ala Ala Lys Lys Gly Cys Leu 580 585 590

Ala Arg Val Lys Lys Leu Ser Ser Pro Asp Asn Val Asn Cys Arg Asp 595 600 605

Thr Gln Gly Arg His Ser Thr Pro Leu His Leu Ala Ala Gly Tyr Asn 610 615 620

Asn Leu Glu Val Ala Glu Tyr Leu Leu Gln His Gly Ala Asp Val Asn 625 630 635 640

Ala Gln Asp Lys Gly Gly Leu Ile Pro Leu His Asn Ala Ala Ser Tyr 645 650 655

Gly His Val Asp Val Ala Ala Leu Leu Ile Lys Tyr Asn Ala Cys Val 660 665 670

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Lys Gly Arg Thr Gln Leu Cys Ala Leu Leu Leu Ala His Gly Ala Asp 690 695 700

Pro Thr Leu Lys Asn Gln Glu Gly Gln Thr Pro Leu Asp Leu Val Ser 705 710 715 720

Ala Asp Asp Val Ser Ala Leu Leu Thr Ala Ala Met Pro Pro Ser Ala 725 730 735

Leu Pro Ser Cys Tyr Lys Pro Gln Val Leu Asn Gly Val Arg Ser Pro 740 745 750

Gly Ala Thr Ala Asp Ala Leu Ser Ser Gly Pro Ser Ser Pro Ser Ser Ser 765

Leu Ser Ala Ala Ser Ser Leu Asp Asn Leu Ser Gly Ser Phe Ser Glu 770

Leu Ser Ser Val Val Ser Ser Ser Gly Thr Glu Gly Ala Ser Ser Leu 785 790 795 800

Glu Lys Lys Glu Val Pro Gly Val Asp Phe Ser Ile Thr Gln Phe Val 805 810 815

Arg Asn Leu Gly Leu Glu His Leu Met Asp Ile Phe Glu Arg Glu Gln 820 825 830

Ile Thr Leu Asp Val Leu Val Glu Met Gly His Lys Glu Leu Lys Glu 835 840 845

Glu Arg Leu Ile Ser Gly Gln Gln Gly Leu Asn Pro Tyr Leu Thr Leu 865 870 875 880

Asn Thr Ser Gly Ser Gly Thr Ile Leu Ile Asp Leu Ser Pro Asp Asp 885 890 895

Lys Glu Phe Gln Ser Val Glu Glu Glu Met Gln Ser Thr Val Arg Glu 900 905 910

His Arg Asp Gly Gly His Ala Gly Gly Ile Phe Asn Arg Tyr Asn Ile 915 920 925

Leu Lys Ile Gln Lys Val Cys Asn Lys Lys Leu Trp Glu Arg Tyr Thr 930 935 940

His Arg Arg Lys Glu Val Ser Glu Glu Asn His Asn His Ala Asn Glu 945 950 955 960

Arg Met Leu Phe His Gly Ser Pro Phe Val Asn Ala Ile Ile His Lys 965 970 975

Gly Phe Asp Glu Arg His Ala Tyr Ile Gly Gly Met Phe Gly Ala Gly 980 985 990

Ile Tyr Phe Ala Glu Asn Ser Ser Lys Ser Asn Gln Tyr Val Tyr Gly
995 1000 1005

Ile Gly Gly Gly Thr Gly Cys Pro Val His Lys Asp Arg Ser Cys 1010 1015 1020

Tyr Ile Cys His Arg Gln Leu Leu Phe Cys Arg Val Thr Leu Gly 1025 1030 1035

Lys Ser Phe Leu Gln Phe Ser Ala Met Lys Met Ala His Ser Pro 1040 1045 1050

Pro Gly His His Ser Val Thr Gly Arg Pro Ser Val Asn Gly Leu 1055 1060 1065

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Leu Ala Leu Leu Leu Ala Gly Pro Gly Leu Leu Leu Arg Leu Leu Ala 50 55 60

Leu Leu Leu Ala Val Ala Ala Ala Arg Ile Met Ser Gly Arg Arg Cys 65 70 75 80

Ala Gly Gly Ala Ala Cys Ala Ser Ala Ala Ala Glu Ala Val Glu

^{*} 85 · 90 95

Pro Ala Ala Arg Glu Leu Phe Glu Ala Cys Arg Asn Gly Asp Val Glu 100 105 110

Arg Val Lys Arg Leu Val Thr Pro Glu Lys Val Asn Ser Arg Asp Thr 115 120 125

Ala Gly Arg Lys Ser Thr Pro Leu His Phe Ala Ala Gly Phe Gly Arg 130 135 140

Arg Asp Asp Gly Gly Leu Ile Pro Leu His Asn Ala Cys Ser Phe Gly 165 170 175

His Ala Glu Val Val Asn Leu Leu Leu Arg His Gly Ala Asp Pro Asn 180 185 190

Ala Arg Asp Asn Trp Asn Tyr Thr Pro Leu His Glu Ala Ala Ile Lys 195 200 205

Gly Lys Ile Asp Val Cys Ile Val Leu Gln His Gly Ala Glu Pro 210 215 220

Thr Ile Arg Asn Thr Asp Gly Arg Thr Ala Leu Asp Leu Ala Asp Pro 225 230 235 240

Ser Ala Lys Ala Val Leu Thr Gly Glu Tyr Lys Lys Asp Glu Leu Leu 245 250 255

Glu Ser Ala Arg Ser Gly Asn Glu Glu Lys Met Met Ala Leu Leu Thr 260 265 270

Pro Leu Asn Val Asn Cys His Ala Ser Asp Gly Arg Lys Ser Thr Pro 275 280 285

Leu His Leu Ala Ala Gly Tyr Asn Arg Val Lys Ile Val Gln Leu Leu 290 295 300

Leu Gln His Gly Ala Asp Val His Ala Lys Asp Lys Gly Asp Leu Val 305 310 315 320

Pro Leu His Asn Ala Cys Ser Tyr Gly His Tyr Glu Val Thr Glu Leu 325 330 335

Leu Val Lys His Gly Ala Cys Val Asn Ala Met Asp Leu Trp Gln Phe 345 Thr Pro Leu His Glu Ala Ala Ser Lys Asn Arg Val Glu Val Cys Ser 360 Leu Leu Ser Tyr Gly Ala Asp Pro Thr Leu Leu Asn Cys His Asn Lys Ser Ala Ile Asp Leu Ala Pro Thr Pro Gln Leu Lys Glu Arg Leu Ala Tyr Glu Phe Lys Gly His Ser Leu Leu Gln Ala Ala Arg Glu Ala 405 410 Asp Val Thr Arg Ile Lys Lys His Leu Ser Leu Glu Met Val Asn Phe 425 Lys His Pro Gln Thr His Glu Thr Ala Leu His Cys Ala Ala Ala Ser Pro Tyr Pro Lys Arg Lys Gln Ile Cys Glu Leu Leu Arg Lys Gly Ala Asn Ile Asn Glu Lys Thr Lys Glu Phe Leu Thr Pro Leu His Val 470 475 Ala Ser Glu Lys Ala His Asn Asp Val Val Glu Val Val Lys His 485 490 Glu Ala Lys Val Asn Ala Leu Asp Asn Leu Gly Gln Thr Ser Leu His 500 505 Arg Ala Ala Tyr Cys Gly His Leu Gln Thr Cys Arg Leu Leu Leu Ser 515 520 Tyr Gly Cys Asp Pro Asn Ile Ile Ser Leu Gln Gly Phe Thr Ala Leu 530 535



550

565

545

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Leu Gly Asn Ser Glu Ala Asp Arg Gln Leu Leu Glu Ala Ala Lys Ala

570

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Asp Val His Ala Lys Asp Lys Gly Gly Leu Val Pro Leu His Asn Ala 625 630 635 635

Cys Ser Tyr Gly His Tyr Glu Val Ala Glu Leu Leu Val Lys His Gly 645 650 655

Ala Val Val Asn Val Ala Asp Leu Trp Lys Phe Thr Pro Leu His Glu 660 665 670

Ala Ala Lys Gly Lys Tyr Glu Ile Cys Lys Leu Leu Gln His 675 680 685

Gly Ala Asp Pro Thr Lys Lys Asn Arg Asp Gly Asn Thr Pro Leu Asp 690 695 700

Leu Val Lys Asp Gly Asp Thr Asp Ile Gln Asp Leu Leu Arg Gly Asp 705 710 715 720

Ala Ala Leu Leu Asp Ala Ala Lys Lys Gly Cys Leu Ala Arg Val Lys
725 730 735

Lys Leu Ser Ser Pro Asp Asn Val Asn Cys Arg Asp Thr Gln Gly Arg
740 745 750

His Ser Thr Pro Leu His Leu Ala Ala Gly Tyr Asn Asn Leu Glu Val 755 760 765

Ala Glu Tyr Leu Leu Gln His Gly Ala Asp Val Asn Ala Gln Asp Lys 770 780

Gly Gly Leu Ile Pro Leu His Asn Ala Ala Ser Tyr Gly His Val Asp 785 790 795 800

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- Lys Trp Ala Phe Thr Pro Leu His Glu Ala Ala Gln Lys Gly Arg Thr 820 825 830
- Gln Leu Cys Ala Leu Leu Leu Ala His Gly Ala Asp Pro Thr Leu Lys 835 840 845
- Asn Gln Glu Gly Gln Thr Pro Leu Asp Leu Val Ser Ala Asp Asp Val 850 855 860
- Ser Ala Leu Leu Thr Ala Ala Met Pro Pro Ser Ala Leu Pro Ser Cys 865 870 875 880
- Tyr Lys Pro Gln Val Leu Asn Gly Val Arg Ser Pro Gly Ala Thr Ala 885 890 895
- Asp Ala Leu Ser Ser Gly Pro Ser Ser Pro Ser Ser Leu Ser Ala Ala 900 905 910
- Ser Ser Leu Asp Asn Leu Ser Gly Ser Phe Ser Glu Leu Ser Ser Val 915 920 925
- Val Ser Ser Ser Gly Thr Glu Gly Ala Ser Ser Leu Glu Lys Lys Glu 930 935 940
- Val Pro Gly Val Asp Phe Ser Ile Thr Gln Phe Val Arg Asn Leu Gly 945 950 955 960
- Leu Glu His Leu Met Asp Ile Phe Glu Arg Glu Gln Ile Thr Leu Asp 965 970 975
- Val Leu Val Glu Met Gly His Lys Glu Leu Lys Glu Ile Gly Ile Asn 980 985 990
- Ala Tyr Gly His Arg His Lys Leu Ile Lys Gly Val Glu Arg Leu Ile 995 1000 1005
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- Gly Ser Gly Thr Ile Leu Ile Asp Leu Ser Pro Asp Asp Lys Glu 1025 1030 1035
- Phe Gln Ser Val Glu Glu Glu Met Gln Ser Thr Val Arg Glu His 1040 1050
- Arg Asp Gly Gly His Ala Gly Gly Ile Phe Asn Arg Tyr Asn Ile

1055 1060 1065

Leu Lys Ile Gln Lys Val Cys Asn Lys Lys Leu Trp Glu Arg Tyr 1070 1075 1080

Thr His Arg Arg Lys Glu Val Ser Glu Glu Asn His Asn His Ala 1085 1090 1095

Asn Glu Arg Met Leu Phe His Gly Ser Pro Phe Val Asn Ala Ile 1100 1105 1110

Ile His Lys Gly Phe Asp Glu Arg His Ala Tyr Ile Gly Gly Met 1115 1120 1125

Phe Gly Ala Gly Ile Tyr Phe Ala Glu Asn Ser Ser Lys Ser Asn 1130 1135 1140

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Arg Val Thr Leu Gly Lys Ser Phe Leu Gln Phe Ser Ala Met Lys 1175 1180 1185

Met Ala His Ser Pro Pro Gly His His Ser Val Thr Gly Arg Pro 1190 1195 1200

Ser Val Asn Gly Leu Ala Leu Ala Glu Tyr Val Ile Tyr Arg Gly 1205 1210 1215

Glu Gln Ala Tyr Pro Glu Tyr Leu Ile Thr Tyr Gln Ile Met Arg 1220 1225 1230

Pro Glu Gly Met Val Asp Gly 1235 1240

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			20	3		1	1	25					30			
Cys	Ser	Phe 35	Gly	His	Ala	Glu	Val 40	Val	Asn	Leu	Leu	Leu 45	Arg	His	Gly	
		33					10					13				
Ala	Asp	Pro	Asn	Ala	Arg	Asp	Asn	Trp	Asn	Tyr	Thr	Pro	Leu	His	Glu	
	50					55					60					
Ala	Ala	Ile	Lvs	Glv	Lvs	Tle	Asn	Val	Cvs	Tle	Val	Len	Leu	Gln	Wie	
65			_75	OI,	70	110	пор	VUI	Cyb	75	vai	пси	пси	GIII	80	
Gly	Ala	Glu	Pro	Thr 85	Ile	Arg	Asn	Thr		Gly	Arg	Thr	Ala		Asp	
				دن					90					95		
Leu	Ala	Asp	Pro	Ser	Ala	Lys	Ala	Val	Leu	Thr	Gly	Glu	Tyr	Lys	Lys	
			100					105			=		110	_	-	

Asp Glu Leu Leu Glu Ser Ala Arg Ser Gly Asn Glu Glu Lys Met Met 120 Ala Leu Leu Thr Pro Leu Asn Val Asn Cys His Ala Ser Asp Gly Arg 130 135 140 Lys Ser Thr Pro Leu His Leu Ala Ala Gly Tyr Asn Arg Val Lys Ile 145 150 155 Val Gln Leu Leu Gln His Gly Ala Asp Val His Ala Lys Asp Lys 165 170 Gly Asp Leu Val Pro Leu His Asn Ala Cys Ser Tyr Gly His Tyr Glu 180 Val Thr Glu Leu Leu Val Lys His Gly Ala Cys Val Asn Ala Met Asp 195 Leu Trp Gln Phe Thr Pro Leu His Glu Ala Ala Ser Lys Asn Arg Val 210 215 Glu Val Cys Ser Leu Leu Leu Ser Tyr Gly Ala Asp Pro Thr Leu Leu 225 235 Asn Cys His Asn Lys Ser Ala Ile Asp Leu Ala Pro Thr Pro Gln Leu 245 Lys Glu Arg Leu Ala Tyr Glu Phe Lys Gly His Ser Leu Leu Gln Ala 260

Bo Cont.

275

Met Val Asn Phe Lys His Pro Gln Thr His Glu Thr Ala Leu His Cys 290 295 300

Ala Arg Glu Ala Asp Val Thr Arg Ile Lys Lys His Leu Ser Leu Glu

- Ala Ala Ser Pro Tyr Pro Lys Arg Lys Gln Ile Cys Glu Leu Leu 305 310 315 320
- Leu Arg Lys Gly Ala Asn Ile Asn Glu Lys Thr Lys Glu Phe Leu Thr 325 330 335
- Pro Leu His Val Ala Ser Glu Lys Ala His Asn Asp Val Val Glu Val 340 345 350

Val Val Lys His Glu Ala Lys Val Asn Ala Leu Asp Asn Leu Gly Gln 355 360 Thr Ser Leu His Arg Ala Ala Tyr Cys Gly His Leu Gln Thr Cys Arg

Leu Leu Ser Tyr Gly Cys Asp Pro Asn Ile Ile Ser Leu Gln Gly 385 395

Phe Thr Ala Leu Gln Met Gly Asn Glu Asn Val Gln Gln Leu Leu Gln 410

Glu Gly Ile Ser Leu Gly Asn Ser Glu Ala Asp Arg Gln Leu Leu Glu 425

Ala Ala Lys Ala Gly Asp Val Glu Thr Val Lys Lys Leu Cys Thr Val 440

Gln Ser Val Asn Cys Arg Asp Ile Glu Gly Arg Gln Ser Thr Pro Leu

His Phe Ala Ala Gly Tyr Asn Arg Val Ser Val Val Glu Tyr Leu Leu 475

Gln His Gly Ala Asp Val His Ala Lys Asp Lys Gly Gly Leu Val Pro

Leu His Asn Ala Cys Ser Tyr Gly His Tyr Glu Val Ala Glu Leu Leu 505

Val Lys His Gly Ala Val Val Asn Val Ala Asp Leu Trp Lys Phe Thr 520

Pro Leu His Glu Ala Ala Ala Lys Gly Lys Tyr Glu Ile Cys Lys Leu 535

Leu Leu Gln His Gly Ala Asp Pro Thr Lys Lys Thr Gly Met Glu Ile 550

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Ser Val Gln Ala Arg Asp Asp Gly Gly Leu Ile Pro Leu His Asn Ala 20 25 30

Cys Ser Phe Gly His Ala Glu Val Val Asn Leu Leu Arg His Gly 35 40 45

Ala Asp Pro Asn Ala Arg Asp Asn Trp Asn Tyr Thr Pro Leu His Glu 50 55 60

Ala Ala Ile Lys Gly Lys Ile Asp Val Cys Ile Val Leu Leu Gln His 65 70 75 80

Gly Ala Glu Pro Thr Ile Arg Asn Thr Asp Gly Arg Thr Ala Leu Asp 85 90 95

Leu Ala Asp Pro Ser Ala Lys Ala Val Leu Thr Gly Glu Tyr Lys Lys
100 105 110

Asp Glu Leu Leu Glu Ser Ala Arg Ser Gly Asn Glu Glu Lys Met Met 115 120 125

Ala Leu Leu Thr Pro Leu Asn Val Asn Cys His Ala Ser Asp Gly Arg 130 135 140

Lys Ser Thr Pro Leu His Leu Ala Ala Gly Tyr Asn Arg Val Lys Ile 145 150 155 160

Val Gln Leu Leu Gln His Gly Ala Asp Val His Ala Lys Asp Lys 165 170 175

Gly Asp Leu Val Pro Leu His Asn Ala Cys Ser Tyr Gly His Tyr Glu 180 185 190

Val Thr Glu Leu Leu Val Lys His Gly Ala Cys Val Asn Ala Met Asp 195 200 205

Leu Trp Gln Phe Thr Pro Leu His Glu Ala Ala Ser Lys Asn Arg Val 215 Glu Val Cys Ser Leu Leu Leu Ser Tyr Gly Ala Asp Pro Thr Leu Leu 230 235 Asn Cys His Asn Lys Ser Ala Ile Asp Leu Ala Pro Thr Pro Gln Leu 245 250 Lys Glu Arg Leu Ala Tyr Glu Phe Lys Gly His Ser Leu Leu Gln Ala Ala Arg Glu Ala Asp Val Thr Arg Ile Lys Lys His Leu Ser Leu Glu Met Val Asn Phe Lys His Pro Gln Thr His Glu Thr Ala Leu His Cys 290 Ala Ala Ser Pro Tyr Pro Lys Arg Lys Gln Ile Cys Glu Leu Leu 315 Leu Arg Lys Gly Ala Asn Ile Asn Glu Lys Thr Lys Glu Phe Leu Thr 330 Pro Leu His Val Ala Ser Glu Lys Ala His Asn Asp Val Val Glu Val 345 Val Val Lys His Glu Ala Lys Val Asn Ala Leu Asp Asn Leu Gly Gln 360 Thr Ser Leu His Arg Ala Ala Tyr Cys Gly His Leu Gln Thr Cys Arg 370 375 Leu Leu Ser Tyr Gly Cys Asp Pro Asn Ile Ile Ser Leu Gln Gly 395 400 Phe Thr Ala Leu Gln Met Gly Asn Glu Asn Val Gln Gln Leu Leu Gln 405 410 Glu Gly Ile Ser Leu Gly Asn Ser Glu Ala Asp Arg Gln Leu Leu Glu 420 425 Ala Ala Lys Ala Gly Asp Val Glu Thr Val Lys Lys Leu Cys Thr Val 435 440 445

Gln Ser Val Asn Cys Arg Asp Ile Glu Gly Arg Gln Ser Thr Pro Leu

450 455

455 460

His Phe Ala Ala Gly Tyr Asn Arg Val Ser Val Val Glu Tyr Leu Leu 465 470 475 480

Gln His Gly Ala Asp Val His Ala Lys Asp Lys Gly Gly Leu Val Pro 485 490 495

Leu His Asn Ala Cys Ser Tyr Gly His Tyr Glu Val Ala Glu Leu Leu 500 505 510

Val Lys His Gly Ala Val Val Asn Val Ala Asp Leu Trp Lys Phe Thr 515 520 525

Pro Leu His Glu Ala Ala Ala Lys Gly Lys Tyr Glu Ile Cys Lys Leu 530 540

Leu Leu Gln His Gly Ala Asp Pro Thr Lys Lys Asn Arg Asp Gly Asn 545 550 555 560

Thr Pro Leu Asp Leu Val Lys Asp Gly Asp Thr Asp Ile Gln Asp Leu 565 570 575

Leu Arg Gly Asp Ala Ala Leu Leu Asp Ala Ala Lys Lys Gly Cys Leu 580 585 590

Ala Arg Val Lys Lys Leu Ser Ser Pro Asp Asn Val Asn Cys Arg Asp 595 600 605

Thr Gln Gly Arg His Ser Thr Pro Leu His Leu Ala Ala Gly Tyr Asn 610 615 620

Asn Leu Glu Val Ala Glu Tyr Leu Leu Gln His Gly Ala Asp Val Asn 625 630 635 640

Ala Gln Asp Lys Gly Gly Leu Ile Pro Leu His Asn Ala Ala Ser Tyr 645 650 655

Gly His Val Asp Val Ala Ala Leu Leu Ile Lys Tyr Asn Ala Cys Val 660 665 670

Asn Ala Thr Asp Lys Trp Ala Phe Thr Pro Leu His Glu Ala Ala Gln
675 680 685

Lys Gly Arg Thr Gln Leu Cys Ala Leu Leu Leu Ala His Gly Ala Asp 690 695 700

Pro Thr Leu Lys Asn Gln Glu Gly Gln Thr Pro Leu Asp Leu Val Ser 710 715 Ala Asp Asp Val Ser Ala Leu Leu Thr Ala Ala Met Pro Pro Ser Ala 725 730 Leu Pro Ser Cys Tyr Lys Pro Gln Val Leu Asn Gly Val Arg Ser Pro 745 Gly Ala Thr Ala Asp Ala Leu Ser Ser Gly Pro Ser Ser Pro Ser Ser 760 Leu Ser Ala Ala Ser Ser Leu Asp Asn Leu Ser Gly Ser Phe Ser Glu 775 Leu Ser Ser Val Val Ser Ser Ser Gly Thr Glu Gly Ala Ser Ser Leu 790 Glu Lys Lys Glu Val Pro Gly Val Asp Phe Ser Ile Thr Gln Phe Val 810 Arg Asn Leu Gly Leu Glu His Leu Met Asp Ile Phe Glu Arg Glu Gln 825 Ile Thr Leu Asp Val Leu Val Glu Met Gly His Lys Glu Leu Lys Glu Ile Gly Ile Asn Ala Tyr Gly His Arg His Lys Leu Ile Lys Gly Val 855 Glu Arg Leu Ile Ser Gly Gln Gln Gly Leu Asn Pro Tyr Leu Thr Leu 870 880 Asn Thr Ser Gly Ser Gly Thr Ile Leu Ile Asp Leu Ser Pro Asp Asp 885 Lys Glu Phe Gln Ser Val Glu Glu Glu Met Gln Ser Thr Val Arg Glu 900 His Arg Asp Gly Gly His Ala Gly Gly Ile Phe Asn Arg Tyr Asn Ile 915

Leu Lys Ile Gln Lys Val Cys Asn Lys Lys Leu Trp Glu Arg Tyr Thr

His Arg Arg Lys Glu Val Ser Glu Glu Asn His Asn His Ala Asn Glu 945 950 955 960

Arg Met Leu Phe His Gly Ser Pro Phe Val Asn Ala Ile Ile His Lys 965 970 975

Gly Phe Asp Glu Arg His Ala Tyr Ile Gly Gly Met Phe Gly Ala Gly 980 985 990

Ile Tyr Leu Ala Glu Asn Ser Ser Lys Ser Asn Gln Tyr Val Tyr Gly
995 1000 1005

Ile Gly Gly Gly Thr Gly Cys Pro Val His Lys Asp Arg Ser Cys 1010 1015 1020

Tyr Ile Cys His Arg Gln Leu Leu Phe Cys Arg Val Thr Leu Gly 1025 1030 1035

Lys Ser Phe Leu Gln Phe Ser Ala Met Lys Met Ala His Ser Pro 1040 1045 1050

Pro Gly His His Ser Val Thr Gly Arg Pro Ser Val Asn Gly Leu 1055 1060 1065

Ala Leu Ala Glu Tyr Val Ile Tyr Arg Gly Glu Gln Ala Tyr Pro 1070 1080

Glu Tyr Leu Ile Thr Tyr Gln Ile Met Arg Pro Glu Gly Met Val 1085 1090 1095

Asp Gly 1100

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Gly Phe Gly Arg Lys Asp Val Val Glu Tyr Leu Leu Gln Asn Gly Ala 1 5 10 15

Ser Val Gln Ala Arg Asp Asp Gly Gly Leu Ile Pro Leu His Asn Ala

- Cys Ser Phe Gly His Ala Glu Val Val Asn Leu Leu Arg His Gly 35 40 45
- Ala Asp Pro Asn Ala Arg Asp Asn Trp Asn Tyr Thr Pro Leu His Glu 50 55 60
- Ala Ala Ile Lys Gly Lys Ile Asp Val Cys Ile Val Leu Leu Gln His 65 70 75 80
- Gly Ala Glu Pro Thr Ile Arg Asn Thr Asp Gly Arg Thr Ala Leu Asp 85 90 95
- Leu Ala Asp Pro Ser Ala Lys Ala Val Leu Thr Gly Glu Tyr Lys Lys
 100 105 110
- Asp Glu Leu Leu Glu Ser Ala Arg Ser Gly Asn Glu Glu Lys Met Met 115
- Ala Leu Leu Thr Pro Leu Asn Val Asn Cys His Ala Ser Asp Gly Arg 130 135 140
- Lys Ser Thr Pro Leu His Leu Ala Ala Gly Tyr Asn Arg Val Lys Ile 145 150 155 160
- Val Gln Leu Leu Gln His Gly Ala Asp Val His Ala Lys Asp Lys
 165 170 175
- Gly Asp Leu Val Pro Leu His Asn Ala Cys Ser Tyr Gly His Tyr Glu 180 185 190
- Val Thr Glu Leu Leu Val Lys His Gly Ala Cys Val Asn Ala Met Asp 195 200 205
- Leu Trp Gln Phe Thr Pro Leu His Glu Ala Ala Ser Lys Asn Arg Val 210 215 220
- Glu Val Cys Ser Leu Leu Leu Ser Tyr Gly Ala Asp Pro Thr Leu Leu 225 230 235 240
- Asn Cys His Asn Lys Ser Ala Ile Asp Leu Ala Pro Thr Pro Gln Leu 245 250 255
- Lys Glu Arg Leu Ala Tyr Glu Phe Lys Gly His Ser Leu Leu Gln Ala 260 265 270

Ala Arg Glu Ala Asp Val Thr Arg Ile Lys Lys His Leu Ser Leu Glu 275 280 285

Met Val Asn Phe Lys His Pro Gln Thr His Glu Thr Ala Leu His Cys 290 295 300

Ala Ala Ala Ser Pro Tyr Pro Lys Arg Lys Gln Ile Cys Glu Leu Leu 305 310 315 320

Leu Arg Lys Gly Ala Asn Ile Asn Glu Lys Thr Lys Glu Phe Leu Thr 325 330 335

Pro Leu His Val Ala Ser Glu Lys Ala His Asn Asp Val Val Glu Val 340 345 350

Val Val Lys His Glu Ala Lys Val Asn Ala Leu Asp Asn Leu Gly Gln 355 360 365

Thr Ser Leu His Arg Ala Ala Tyr Cys Gly His Leu Gln Thr Cys Arg 370 375 380

Leu Leu Ser Tyr Gly Cys Asp Pro Asn Ile Ile Ser Leu Gln Gly 385 390 395

Phe Thr Ala Leu Gln Met Gly Asn Glu Asn Val Gln Gln Leu Leu Gln 405 410 415

Glu Gly Ile Ser Leu Gly Asn Ser Glu Ala Asp Arg Gln Leu Leu Glu 420 425 430

Ala Ala Lys Ala Gly Asp Val Glu Thr Val Lys Lys Leu Cys Thr Val
435 440 445

Gln Ser Val Asn Cys Arg Asp Ile Glu Gly Arg Gln Ser Thr Pro Leu 450 455 460

His Phe Ala Ala Gly Tyr Asn Arg Val Ser Val Val Glu Tyr Leu Leu 465 470 475 480

Gln His Gly Ala Asp Val His Ala Lys Asp Lys Gly Gly Leu Val Pro 485 490 495

Leu His Asn Ala Cys Ser Tyr Gly His Tyr Glu Val Ala Glu Leu Leu
500 505 510

Val Lys His Gly Ala Val Val Asn Val Ala Asp Leu Trp Lys Phe Thr 515 Leu His Glu Ala Ala Ala Lys Gly Lys Tyr Glu Ile Cys Lys Leu 530 Leu Leu Gln His Gly Ala Asp Pro Thr Lys Lys Asn Arg Asp Gly Asn

Thr Pro Leu Asp Leu Val Lys Asp Gly Asp Thr Asp Ile Gln Asp Leu

555

570

550

Leu Arg Gly Asp Ala Ala Leu Leu Asp Ala Ala Lys Lys Gly Cys Leu 580 585 590

Ala Arg Val Lys Lys Leu Ser Ser Pro Asp Asn Val Asn Cys Arg Asp 595 600 605

Thr Gln Gly Arg His Ser Thr Pro Leu His Leu Ala Ala Gly Tyr Asn 610 615 620

Asn Leu Glu Val Ala Glu Tyr Leu Leu Gln His Gly Ala Asp Val Asn 625 630 635 640

Ala Gln Asp Lys Gly Gly Leu Ile Pro Leu His Asn Ala Ala Ser Tyr 645 650 655

Gly His Val Asp Val Ala Ala Leu Leu Ile Lys Tyr Asn Ala Cys Val 660 665 670

Asn Ala Thr Asp Lys Trp Ala Phe Thr Pro Leu His Glu Ala Ala Gln 675 680 685

Lys Gly Arg Thr Gln Leu Cys Ala Leu Leu Leu Ala His Gly Ala Asp 690 695 700

Pro Thr Leu Lys Asn Gln Glu Gly Gln Thr Pro Leu Asp Leu Val Ser 705 710 715 720

Ala Asp Asp Val Ser Ala Leu Leu Thr Ala Ala Met Pro Pro Ser Ala 725 730 735

Leu Pro Ser Cys Tyr Lys Pro Gln Val Leu Asn Gly Val Arg Ser Pro 740 745 750

Gly Ala Thr Ala Asp Ala Leu Ser Ser Gly Pro Ser Ser Pro Ser Ser

760 755 ` 765

Leu Ser Ala Ala Ser Ser Leu Asp Asn Leu Ser Gly Ser Phe Ser Glu 770 775 780

Leu Ser Ser Val Val Ser Ser Ser Gly Thr Glu Gly Ala Ser Ser Leu 785 790 795

Glu Lys Lys Glu Val Pro Gly Val Asp Phe Ser Ile Thr Gln Phe Val 805

Arg Asn Leu Gly Leu Glu His Leu Met Asp Ile Phe Glu Arg Glu Gln 820

Ile Thr Leu Asp Val Leu Val Glu Met Gly His Lys Glu Leu Lys Glu

Ile Gly Ile Asn Ala Tyr Gly His Arg His Lys Leu Ile Lys Gly Val 850 855

Glu Arg Leu Ile Ser Gly Gln Gln Gly Leu Asn Pro Tyr Leu Thr Leu 870

Asn Thr Ser Gly Ser Gly Thr Ile Leu Ile Asp Leu Ser Pro Asp Asp

Lys Glu Phe Gln Ser Val Glu Glu Glu Met Gln Ser Thr Val Arg Glu 900

His Arg Asp Gly Gly His Ala Gly Gly Ile Phe Asn Arg Tyr Asn Ile 915

Leu Lys Ile Gln Lys Val Cys Asn Lys Lys Leu Trp Glu Arg Tyr Thr 930 935

His Arg Arg Lys Glu Val Ser Glu Glu Asn His Asn His Ala Asn Glu 955

Arg Met Leu Phe His Gly Ser Pro Phe Val Asn Ala Ile Ile His Lys 965 970

Gly Phe Asp Glu Arg His Ala Tyr Ile Gly Gly Met Phe Gly Ala Gly 985

Ile Tyr Phe Ala Glu Asn Ser Ser Lys Ser Asn Gln Tyr Val Tyr Gly 1000 1005

Ile Gly Gly Gly Thr Gly Cys Pro Val His Lys Asp Arg Ser Cys Tyr Ile Cys His Arg Gln Leu Leu Phe Cys Arg Val Thr Leu Gly 1030 Lys Ser Phe Leu Gln Phe Ser Ala Met Lys Met Ala His Ser Pro 1045 Pro Gly His His Ser Val Thr Gly Arg Pro Ser Val Asn Gly Leu 1055 1060 Ala Leu Ala Ala Tyr Val Ile Tyr Arg Gly Glu Gln Ala Leu Ser 1070 1075 <210> 11 <211> 9 <212> PRT <213> Unknown <220> <223> cyclin A destruction box <400> 11 Arg Thr Val Leu Gly Val Ile Gly Asp <210> 12 <211> 9 <212> PRT <213> Unknown <220> <223> Cyclin B1 destruction box <400> 12 Arg Thr Ala Leu Gly Asp Ile Gly Asn <210> 13 <211> 27 <212> PRT <213> Rattus sp. <400> 13 Tyr Met Thr Val Ser Ile Ile Asp Arg Phe Met Gln Asp Ser Cys Val

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Asp Arg Phe Met Gln Asn Ser Cys Val Pro Lys Lys
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Leu Leu Gln Glu Thr Met Tyr Met Thr Val Ser
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Val Gly Ile Thr Ala Leu Leu Leu Ala Ser Lys
           20
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<212> PRT
<213> Mus sp.
<400> 17
Met Ser Val Leu Arg Gly Lys Leu Gln Leu Val Gly Thr Ala Ala Met
1 5
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Pro Lys Lys Met Leu Glin Leu Val Gly Val Thr

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